



Letter to the Editor

ECLS indication for a case of stress myocardialopathy associated with severe asthma

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1. Introduction

Severe asthma is a life threatening pathology, not only because of respiratory distress, but also due to haemodynamic failure, and possible cardiac arrest. Though right ventricular failure is the more frequent presentation, stress myocardialopathy can occur during severe asthma. Massive use of $\beta 2$ agonists administered during an asthma attack induces a negative inotropic reaction, responsible for transient left ventricular failure. In case of refractory severe asthma or haemodynamic shock, ECLS can provide a bridge to recovery, until the asthma attack and stress myocardialopathy can be resolved.

2. Case report

A 29-year-old-woman was hospitalized for critical asthma syndrome and cardiogenic shock. Her medical history mainly included asthma, treated with formoterol and inhaled momethasone, without previous hospitalization or severe decompensation, and a nephrectomy (nephroblastoma). Three pregnancies without any cardiac or respiratory decompensation were known.

In October 2013, the patient consulted her physician for a 24-h history of decompensating asthma. Her ordinary treatment was not efficient. As he noted consciousness disorders, her physician called the emergency medical service. The patient was intubated and required $0.38 \mu\text{g/kg/min}$ norepinephrine support because of haemodynamic collapse. She was transported to a regional hospital. In the intensive care unit, she presented a major bronchospasm, pH was 7.06, pCO_2 was 120 mmHg and $\text{PaO}_2/\text{FiO}_2$ 95. Despite adapted sedation and curarisation, ventilation was extremely difficult, plateau pressure reached 60 cmH_2O for 6 ml/kg (ideal body weight) tidal volume; intrinsic PEEP was 13 cmH_2O . Maximal treatment for severe asthma was initiated: inhaled $\beta 2$ agonist (salbutamol) each hour, inhaled anticholinergic drugs (ipratropium bromide) every 3 hours, intravenous salbutamol, corticoids, ketamine, magnesium sulphate, epinephrine, and

ventilation with sevoflurane. A transthoracic echocardiography showed, paradoxically, a large and global hypokinesia and a ballooned left ventricle (LVEF 20%) and thin right cavities with normal wall motion. Cardiac markers were abnormal with an increase of troponin Ic ($2.64 \mu\text{g/l}$ (h0) and then a peak of $8.64 \mu\text{g/l}$ (h10)). Haemodynamics were unstable and the patient required inotropic and pressor support ($1.3 \mu\text{g/kg/min}$ intravenous epinephrine, $0.8 \mu\text{g/kg/min}$ norepinephrine and then $7.6 \mu\text{g/kg/min}$ dobutamine). Because of severe haemodynamic shock and no respiratory improvement (pH 6.95 after 2 hours, PaCO_2 136 mmHg and $\text{PaO}_2/\text{FiO}_2$ 90), veno-arterial ECLS was initiated after femoral cannulation at the bedside, and the patient was transferred to the intensive care unit of the University Hospital of Lyon. The femoro-femoral ECLS output was 2.9 l/min. The patient benefited from lung protective ventilation (plateau pressure $<25 \text{ cmH}_2\text{O}$, tidal volume 360 ml (i.e. 6 ml/kg of ideal body weight)). ECLS parameters were fresh gas flow: 3.5 l/min, fraction of inspired oxygen (FiO_2): 50%, ECLS flow: 2.9 l/min. Trans-oesophageal echocardiography confirmed an isolated left ventricular dysfunction. The left ventricle was ballooned without basal hyperkinesia, while right ventricular contractility was normal. The initial electrocardiogram showed an ST segment depression of the inferior walls. Emergency coronarography was performed but was normal. Six hours after ECLS implantation, the situation improved: pH and PaO_2 were back to normal. She developed multi-organ failure, with acute hepatic failure (prothrombin ratio 34%) and acute renal failure. She required extra-renal purification. At day 2, a bronchial fibroscopy revealed purulent secretion in the right upper and middle pulmonary lobe. Procalcitonin was $29 \mu\text{g/l}$. However, infectious investigations only revealed positive serological results for rhinovirus and adenovirus. The patient was treated by levofloxacin and ceftriaxone for 5 days as an empiric therapy. Epinephrine could be stopped at day 1 and norepinephrine at day 2. Paralysis was stopped 5 days after the admission and ECLS was explanted 7 days later as the cardiac dysfunction resolved (LVEF 40%) with dobutamine support ($3 \mu\text{g/kg/min}$). Dobutamine was stopped 24 hours later. There was no complication associated with ECLS. Tracheal extubation was performed at day 9. She was still dialyzed at her discharge from the intensive care unit (Fig. 1).

3. Discussion

In a study published in 2006 concerning patients hospitalized for exacerbated asthma in the United States, the overall mortality was 0.5% but reached 7% for patients with mechanical ventilation. Mortality was higher for patients over the age of 35 [1].

During severe asthma, treatment intensification is well known [2,3]. However, the position of circulatory support still needs to be defined. Some authors have questioned the interest of extracorporeal removal of CO_2 (ECCO₂-R) [3], but the position of ECLS is not clear. However, several cases of ECLS use for asthmatic rescue have

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Time from admission in intensive care (hour)	h0	h4	h8	h12	h16
pH	6.95	7.00	7.16	7.22	7.37
PaCO ₂ (mmHg)	84	136	58	21	18
Pinsp (cmH ₂ O)	58	68	18	20	18



Fig. 1. Evolution from initiation of mechanical ventilation to initiation of extracorporeal life support (ECLS).

been described [4,5]. A retrospective study concerning acute respiratory failure needing ECLS, found only 1.9% cases related to asthma [6]. Mainly, there were veno-venous (VV) cases of ECLS and rarely veno-arterial cases. Survival rate during acute respiratory failure was better for severe asthma compared to other cases (83 versus 64%). Such results are probably due to the reversible nature of bronchospasm and the absence of detrimental effects on lung parenchyma. There was the same percentage of complications specifically due to ECLS in all groups. However, no study precisely identified the indication criteria for ECLS. Currently, there is no factor that can predict how long a bronchospasm will last; in order to select patients for whom the risk/benefit balance will be positive, except in the case of cardiorespiratory arrest or intractable right ventricular failure.

Surprisingly, the patient presented an isolated left ventricular failure. Several hypotheses can explain this clinical state. First, an ischaemic injury is a possibility because of an acute onset associated with increased cardiac enzyme concentrations (troponin I: 8.64 µg/l) and because of electrocardiographic changes. However, the patient's age, the absence of cardiovascular risk factors and a normal angiogram eliminate this assumption. Second, myocarditis could also be suspected, because of the initial inflammatory syndrome, the patient's age and the global left ventricular failure. All infectious investigations were negative, electrocardiographic changes are not in favour of this hypothesis, nor the low increase of troponin. Consequently, the most probable hypothesis was stress myocardopathy due to an adrenergic outflow linked to the stress of the respiratory failure, the use of β2 agonists and high doses of epinephrine. The quick reversibility of the left ventricular failure reinforces this hypothesis.

Several authors have linked asthma to stress myocardopathy [7,8]. The main pathophysiological mechanism is probably a massive use of β2 agonists during the asthma attack. β2 agonists would act on the cardiac receptor β as exogenous catecholamines. High doses of catecholamines would trigger a switch in intracellular signal trafficking in ventricular cardiomyocytes via β receptors and induce a negatively inotropic reaction [9]. Beta-receptors are mainly present on the apical myocardium. This phenomenon would explain the typical aspect of Takotsubo syndrome (abnormalities of apical motility and hypercontractility of the basal segments).

In 1991, Dote et al. described Takotsubo syndrome as an acute, transient cardiac dysfunction associated with ischaemic electrocardiographic changes without coronary abnormalities [10]. Typical Takotsubo syndrome [11,12] is described as a reversible left ventricular ballooning with abnormalities of apical motility and hypercontractility of the basal segments, sometimes associated with a left ventricular outflow tract obstruction. However, certain authors have reported electrical [13] and morphological [14] variations. Following the Mayo Clinic criteria, basal hyperkinesia is not an essential criteria for the diagnosis of Takotsubo syndrome. The diagnosis is based on abnormal mobility of the middle and

apical regions of the left ventricle [15]. A clinical review has identified 30% of atypical forms, with ventricular dysfunctions in different territories [11]. Atypical forms are more common for premenopausal women with few cardiovascular risk factors. Generally, cardiac dysfunction is less important, electrocardiographic signs are poorer as well as the increase cardiac enzymes [14].

Only a few cases of stress myocardopathy needing ECLS have been reported in the literature [16,17]. Stress myocardopathy complicated by cardiogenic shock represents 4.2% of cases [18]. Because of its excellent prognosis (1 to 2% in hospital mortality [18]) and of the reversibility of the cardiac dysfunction, stress myocardopathy is a good indication for ECLS. However, due to potentially serious complications, ECLS remains a rescue therapy in case of refractory cardiogenic shock, rather than a first-line treatment.

4. Conclusion

This case report illustrates a little-known complication of severe asthma: stress myocardopathy, and its different clinical descriptions. ECLS can be an efficient rescue therapy for medical pathologies requiring transitory haemodynamic support such as severe asthma or stress myocardopathy, after considering the risk/benefit balance.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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Consent for publication of the report has been granted by the patient.

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